1644

Dkt. 60772-PCT-US/JPW/GJG/CSN

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Rina Aharoni et al. Examiner: A. DeCloux

U.S. Serial No.: 09/768,872 Group Art Unit: 1644

Filed : January 23, 2001

For : TREATMENT OF AUTOIMMUNE CONDITIONS WITH COPOLYMER 1 RELATED COPOLYMERS AND PEPTIDES

1185 Avenue of the Americas
New York, New York 10036
August 13, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT PURSUANT TO 37 C.F.R. §1.97(b)(3)

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following publications which are listed again on the attached Form PTO-1449 (**Exhibit A**) and copies of References Items 1-41 **(Exhibits 1-37)** are enclosed.

This Supplemental Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Supplemental Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b)(3).

For the convenience of the Examiner, applicants point out that Reference Items 9, 11-13, 21, and 25 were cited in the June 11, 2002 European Search Report attached hereto as **Exhibit B** in the counterpart European application. Applicants also point out that Reference Items 26-34, 36-37, and 39-41 were cited in the counterpart Australian application. In addition, applicants point out that Reference Items 1, 3, 16, 35, and 38 were cited in the

counterpart New Zealand application.

Applicants also point out that several of the listed references are counterparts of each other and are cumulative. Therefore, in accordance with 37 C.F.R. § 1.98(c), a counterpart of a reference is identified after the cite to the reference, but a copy of only one of the counterparts is being provided. Upon request, applicants will provide the Examiner with copies of any reference that is reasonably available to them.

1. U.S. Patent No. 5,554,372, issued September 10, 1996 (Hunter et al.) **(Exhibit 1)**;

2. U.S. Patent No. 5,623,052, issued April 22, 1997 (McLean et al.) **(Exhibit 2)**;

3. U.S. Patent No. 5,734,023, issued March 31, 1998 (Bishwajit et al.) **(Exhibit 3)**;

4. U.S. Patent No. 5,886,156, issued March 23, 1999 (McLean et al.) **(Exhibit 4)**;

5. U.S. Serial No. 09/487,793, filed January 20, 2000 **(Exhibit 5)**;

6. U.S. Serial No. 09/620,216, filed July 20, 2000 **(Exhibit 6)**;

7. U.S. Serial No. 09/765,301. Applicants point out that this reference is a counterpart of PCT International Application No. PCT/US01/02118 (WO 01/93893) (Exhibit 12);

8. U.S. Serial No. 09/765,644. Applicants point out that this reference is a counterpart of PCT International Application No. PCT/US01/02117 (WO 01/52878) (Exhibit 11);

9. PCT International Application No. PCT/EP91/01420 (WO 92/02543), published February 20, 1992 (Gaeta et al.) **(Exhibit 7)**;

10. PCT International Application No. PCT/US93/06249 (WO 94/03484), published February 17, 1994 (McLean et al.). Applicants point out that this reference is a counterpart of U.S. Patent No. 5,623,052 (Exhibit 2) and U.S. Patent No. 5,886,156 (Exhibit 4);

11. PCT International Application No. PCT/US94/05632 (WO 94/26774), published November 24, 1994 (Alexander et al.) **(Exhibit 8)**;

12. PCT International Application No. PCT/US95/04121 (WO 95/26980), published October 12, 1995 (Hackett et al.) **(Exhibit 9)**;

13. PCT International Application No. PCT/US94/05697 (WO 95/31997), published November 30, 1995 (Reid et al.) **(Exhibit 10)**;

14. PCT International Application No. PCT/US01/02117 (WO 01/52878), published July 26, 2001 (Eisenbach-Schwartz et al.) **(Exhibit 11)**;

15. PCT International Application No. PCT/US01/02118 (WO 01/93893), published December 13, 2001 (Eisenbach-Schwartz et al.) **(Exhibit 12)**;

16. New Zealand Patent Application No. 254996, published August 28, 1996 (Merrell Dow Pharmaceuticals, Inc.). Applicants point out that this reference is a counterpart of U.S. Patent No. 5,623,052 (Exhibit 2) and U.S. Patent No. 5,886,156 (Exhibit 4);

17. Fridkis-Hareli et al., "Synthetic Peptides that Inhibit Binding of the Collagen Type II 261-273 Epitope to Rheumatoid Arthritis-Associated HLA-DR1 and DR4 Molecules and Collagen-Specific T-cell Responses", Database HCAPLUS on STN, Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark, HCAPLUS AN: 2000:455053, Human Immunology, 2000, 61(7): 640-650 (Abstract) **(Exhibit 13)**;

18. Henry, Celia M., "Special Delivery", Chem. and Eng. News, Sept. 18, 2000, 49-54 **(Exhibit 14)**;

19. Cazzato, et al., "Treatment of Multiple Sclerosis. The Present and the Future. Study Group on Diagnosis and Therapy of Multiple Sclerosis"; Database Medline on STN, Instituto do Clinica Neurologica, Universit`a, Trieste, Italy: Medline AN: 2000060325, Recent Progressi in Medicina, October 1999, 90(10): 538-544 (Abstract) **(Exhibit 15)**;

20. Cohen, "Fundamental Immunology", Systemic Autoimmunity, 4th Ed., 1999, 1083 **(Exhibit 16)**;

21. Fridkis-Hareli et al., "Binding of random copolymers of three amino acids to class II MHC molecules", Intl.

Immunol., 1999, 11(5): 635-641 **(Exhibit 17)**;

22. Kepsutlu et al., "Evaluation of Chitosan Used as an Excipient in Tablet Formulations", Database HCAPLUS on STN, Department of Pharmaceutical Technology, Gulhane Military Medical Academy, Ankara, 06018, Turkey, HCAPLUS AN: 1999: 590411, Acta. Pol. Pharm. 1999, 56(3): 27-235 (Abstract) **(Exhibit 18)**;

23. Prat, et al., "Lymphocyte Migration and Multiple Sclerosis: Relation with Disease Course and Therapy," Ann. Neurol., 1999, 46: 253-256 **(Exhibit 19)**;

24. Fridkis-Hareli, et al., "Synthetic Amino Acid Copolymers that Bind to HLA-DR Proteins and Inhibit Type II Collagen-reactive T Cell Clones", Proc. Natl. Acad. Sci., October 1998, 95: 12528-12531 **(Exhibit 20)**;

25. Li et al., "Glatiramer acetate blocks the activation of THP-1 cells by interferon-γ", Eur. J. Pharmacol., 1998, 342: 303-310 **(Exhibit 21)**;

26. Zisman et al., "Dichotomy between the T and the B cellepitopes of the synthetic polypeptide (T,G)-A--L", Eur. J. Immunol., 1994, 24(10): 2497-2505 (Abstract) **(Exhibit 22)**;

27. Deeb et al., "Comparision of Freund's and Ribi adjuvants for inducing antibodies to the synthetic antigen (TG)-AL in rabbits", J. Immunol. Methods, 1992, 152(1): 105-113 (Abstract) **(Exhibit 23)**;

28. Zisman et al., "Direct binding of a synthetic multichain

polypeptide to Class II Major Histocompatibility Complex molecules on Antigen-Presenting Cells and stimulation of a specific T-cell line require processing of the polypeptide", Proc. Natl. Acad. Sci. USA, 1991, 88(21): 9732-9742 (Abstract) **(Exhibit 24)**;

29. Matsunaga et al., "Complementation of Class II A alleles in the immune response to (Glu-Lys-Tyr) polymers", Yokohama Med. Bull., 1988, 39(1-2): 9-19 (Abstract) **(Exhibit 25)**;

30. De Kruyff et al., "Analysis of T Cell Responses to Poly-L (GluLys) at the Clonal Level. I. Presence of Responsive Clones in Nonresponder Mice", Eur. J. Immunol., 1987, 17 (8): 1115-1120 (Abstract) **(Exhibit 26)**;

31. Lai et al., "Complementation of Class II A alleles in the immune response to (GluLysTyr) polymers", Exp. Clin. Immunogenet., 1986, 3(1): 38-48 (Abstract) **(Exhibit 27)**;

32. Lai et al., "Monoclonal T cell responses to two epitopes on a single immunogen controlled by two distinct genes", J. Immunol., 1986, 136(10): 3799-3804 (Abstract) **(Exhibit 28)**;

33. Trannoy et al., "Epitope-specific regulation of the T cell repertoire: carrier recognition in association with I-E or I-A does not influence the restriction of hapten-specific T cells", Eur. J. Immunol., 1985, 15(12): 1215-1221 (Abstract) **(Exhibit 29)**;

34. Falo et al., "Analysis of antigen presentation by metabolically inactive accessory cells and their isolated membranes", Proc. Natl. Acad. Sci. USA, 1985, 82(19): 6647-6651 (Abstract) **(Exhibit 30)**;

35. Babu et al., "Ir gene control of T and B Cell Responses to Determinants in (Glu Lys Ala) Terpolymer", J. Immunogenet., 1984, 11(3-4): 251-254 **(Exhibit 31)**;

36. Babu et al., "Reevaluation of response patterns of nonresponder mice to GLPhe polymers", Immunogen., 1983, 18(1): 97-100 (Abstract) **(Exhibit 32)**;

37. Herzenberg et al., "Lack of immune response gene control for induction of epitope-specific suppression by TGAL antigen", Nature, 1982, 295: 329-331 (Abstract) **(Exhibit 33)**;

38. Baxevanis et al., "Genetic Control of T-Cell Proliferative Responses to Poly ($Glu^{40}Ala^{60}$) and Poly ($Glu^{51}Lys^{34}Tyr^{15}$): Subregion-Specific Inhibition of the Responses with Monoclonal Ia Antibodies", Immunogenetics, 1980, 11: 617-628 **(Exhibit 34)**;

39. Maurer et al., "Interpretations of immune responses of mice to poly(Glu60Lys40), its modified derivatives, and the terpolymers poly (Glu55Lys37Leu8) and poly (Glu56Lys37Ser7)", Clin. Immunol. Immunopathol., 1980, 15(3): 344-356 (Abstract) **(Exhibit 35)**;

40. Ju et al., "Idiotypic analysis of antibodies against the terpolymer L-glutamic acid 60-L-alanine30-L-tyrosine10 (GAT). IV. Induction of CGAT idiotype following immunization with various synthetic polymers containing glutamic acid and tyrosine", Eur. J. Immunol., 1979, 9(7): 553-560 (Abstract) **(Exhibit 36)**; and

41. Schwartz et al., "Gene complementation in the T lymphocyte proliferative response to poly (Glu57Lys38Tyr5): Evidence for effects of polymer handling and gene dosage", J. Immunol., 1979, 123(1): 272-278 (Abstract) **(Exhibit 37)**.

Applicants request that the Examiner review the publications and make them of record in the subject application.

If a telephone interview would be of assistance in advancing8 prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby give to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231

8/13/02
John P. White Date
Reg. No. 28,678

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 60772-PCT-US	Serial No. 09/768,872
		Applicants Rina Aharoni, et al.	
	INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Filing Date January 23, 2001	Group Art Unit 1644

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	US	5 5 5 4 3 7 2	9/10/96	Hunter et al.			
	US	5 6 2 3 0 5 2	4/22/97	McLean et al.			
	US	5 7 3 4 0 2 3	3/31/98	Bishwajit et al.			
	US	5 8 8 6 1 5 6	3/23/99	McLean et al.			
✓	US	09 4 8 7 7 9 3	1/20/00				
✓	US	09 6 2 0 2 1 6	7/20/02				
	US	09 7 6 5 3 0 1					
	US	09 7 6 5 6 4 4					

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	NZ	2 5 4 9 9 6	8/28/96	New Zealand				
	WO	9 2 0 2 5 4 3	2/20/92	Europe				
	WO	9 4 0 3 4 8 4	2/17/94	US				
	WO	9 4 2 6 7 7 4	11/24/94	US				
	WO	9 5 2 6 9 8 0	10/12/95	US				
	WO	9 5 3 1 9 9 7	11/30/95	US				
	WO	0 1 5 2 8 7 8	7/26/01	US				
	WO	0 1 9 3 8 9 3	12/3/01	US				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		Fridkis-Hareli et al., "Synthetic Peptides that Inhibit Binding of the Collagen Type II 261-273 Epitope to Rheumatoid Arthritis-Associated HLA-DR1 and DR4 Molecules and Collagen-Specific T-cell Responses", Database HCAPLUS on STN, Department of Clinical Immunology, Aarhus University Hospital, Aarhus, Denmark, HCAPLUS AN: 2000:455053, Human Immunology, 2000, 61(7): 640-650 (Abstract)
		Henry, Celia M., "Special Delivery", Chem. and Eng. News, Sept. 18, 2000, 49-54
		Cazzato, et al., "Treatment of Multiple Sclerosis. The Present and the Future. Study Group on Diagnosis and Therapy of Multiple Sclerosis", Database Medline on STN, Instituto do Clinica Neurologica, Universita a, Trieste, Italy: Medline AN: 2000060325, Recent Progressi in Medicina, October 1999, 90(10): 538-544 (Abstract)

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty Docket No. 60772-PCT-US	Serial No. 09/76[illegible]872
	INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Applicants Rina Aharoni, et al.	
		Filing Date January 23, 2001	Group Art Unit 1644

OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

		Cohen, "Fundamental Immunology", Systemic Autoimmunity, 4th Ed., 1999, 1083
		Fridkis-Hareli et al., "Binding of random copolymers of three amino acids to class II MHC molecules", Intl. Immunol., 1999, 11(5): 635-641
		Kepsutlu et al., "Evaluation of Chitosan Used as an Excipient in Tablet Formulations", Database HCAPLUS on STN, Department of Pharmaceutical Technology, Gulhane Military Medical Academy, Ankara, 06018, Turkey, HCAPLUS AN: 1999: 590411, Acta. Pol. Pharm. 1999, 56(3): 227-235 (Abstract)
		Prat, et al., "Lymphocyte Migration and Multiple Sclerosis: Relation with Disease Course and Therapy," Ann. Neurol., 1999, 46: 253-256
		Fridkis-Hareli, et al., "Synthetic Amino Acid Copolymers that Bind to HLA-DR Proteins and Inhibit Type II Collagen-reactive T Cell Clones", Proc. Natl. Acad. Sci., October 1998, 95: 12528-12531
		Li et al., "Glatiramer acetate blocks the activation of THP-1 cells by interferon-γ", Eur. J. Pharmacol., 1998, 342: 303-310
		Zisman et al., "Dichotomy between the T and the B cellepitopes of the synthetic polypeptide (T,G)-A--L", Eur. J. Immunol., 1994, 24(10): 2497-2505 (Abstract)
		Deeb et al., "Comparision of Freund's and Ribi adjuvants for inducing antibodies to the synthetic antigen (TG)-AL in rabbits", J. Immunol. Methods, 1992, 152(1): 105-113 (Abstract)
		Zisman et al., "Direct binding of a synthetic multichain polypeptide to Class II Major Histocompatibility Complex molecules on Antigen-Presenting Cells and stimulation of a specific T-cell line require processing of the polypeptide", Proc. Natl. Acad. Sci. USA, 1991, 88(21): 9732-9742 (Abstract)
		Matsunaga et al., "Complementation of Class II A alleles in the immune response to (Glu-Lys-Tyr) polymers", Yokohama Med. Bull., 1988, 39(1-2): 9-19 (Abstract)
		De Kruyff et al., "Analysis of T Cell Responses to Poly-L (GluLys) at the Clonal Level. I. Presence of Responsive Clones in Nonresponder Mice", Eur. J. Immunol., 1987, 17 (8): 1115-1120 (Abstract)
		Lai et al., "Complementation of Class II A alleles in the immune response to (GluLysTyr) polymers", Exp. Clin. Immunogenet., 1986, 3(1): 38-48 (Abstract)
		Lai et al., "Monoclonal T cell responses to two epitopes on a single immunogen controlled by two distinct genes", J. Immunol., 1986, 136(10): 3799-3804 (Abstract)
		Trannoy et al., "Epitope-specific regulation of the T cell repertoire: carrier recognition in association with I-E or I-A does not influence the restriction of hapten-specific T cells", Eur. J. Immunol., 1985, 15(12): 1215-1221 (Abstract)
		Falo et al., "Analysis of antigen presentation by metabolically inactive accessory cells and their isolated membranes", Proc. Natl. Acad. Sci. USA, 1985 82 (19): 6647-6651 (Abstract)

EXAMINER	DATE CONSIDERED

***EXAMINER:** Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 60772-PCT-US	Serial No. 09/768,872
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)	Applicants Rina Aharoni, et al.	
	Filing Date January 23, 2001	Group Art Unit 1644

OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

		Babu et al., "Ir gene control of T and B Cell Responses to Determinants in (Glu Lys Ala) Terpolymer", J. Immunogenet., 1984, 11(3-4): 251-254
		Babu et al., "Reevaluation of response patterns of nonresponder mice to GLPhe polymers", Immunogen., 1983, 18(1): 97-100 (Abstract)
		Herzenberg et al., "Lack of immune response gene control for induction of epitope-specific suppression by TGAL antigen", Nature, 1982, 295: 329-331 (Abstract)
		Baxevanis et al., "Genetic Control of T-Cell Proliferative Responses to Poly ($Glu^{40}Ala^{60}$) and Poly ($Glu^{51}Lys^{34}Tyr^{15}$): Subregion-Specific Inhibition of the Responses with Monoclonal Ia Antibodies", Immunogenetics, 1980, 11: 617-628
		Maurer et al., "Interpretations of immune responses of mice to poly(Glu60Lys40), its modified derivatives, and the terpolymers poly (Glu55Lys37Leu8) and poly (Glu56Lys37Ser7)", Clin. Immunol. Immunopathol., 1980, 15(3): 344-356 (Abstract)
		Ju et al., "Idiotypic analysis of antibodies against the terpolymer L-glutamic acid 60-L-alanine30-L-tyrosine10 (GAT). IV. Induction of CGAT idiotype following immunization with various synthetic polymers containing glutamic acid and tyrosine", Eur. J. Immunol., 1979, 9(7): 553-560 (Abstract)
		Schwartz et al., "Gene complementation in the T lymphocyte proliferative response to poly (Glu57Lys38Tyr5): Evidence for effects of polymer handling and gene dosage", J. Immunol., 1979, 123(1): 272-278 (Abstract)

EXAMINER	DATE CONSIDERED

***EXAMINER:** Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.